UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/331,376	06/18/1999	OYSTEIN FODSTAD	7885.65USWO	1579

23552 7590 09/10/2004

MERCHANT & GOULD PC
P.O. BOX 2903
MINNEAPOLIS, MN 55402-0903

EXAMINER	
DAVIS, MINH TAM B	

ART UNIT	PAPER NUMBER
1642	

DATE MAILED: 09/10/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/331,376	FODSTAD ET AL.	
	Examiner	Art Unit	
	MINH-TAM DAVIS	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 July 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-4,6-11 and 13-18* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4,6-11 and 13-18* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Applicant adds new claim 18, which is related to claims 1-4, 6-11, 13-17 and is not new matter.

Accordingly, claims 1-4, 6-11, 13-18 are being examined.

The following are the remaining rejections.

REJECTION UNDER 35 USC 103

Rejection under 35 USC 103 of claims 1-4, 6-11, 13-17 pertaining to being obvious over Hajek et al, in view of Fodstad et al, and O'briant remains for reasons already of record in paper of 04/05/04.

New claim 18 is rejected for the same reasons already of record.

A. Applicant argues that in the claimed method, the suspension contains different particles, with different antibodies, all directed to the same cell. Applicant submits the electromicrograph of Exhibit A showing different particles bound to the surface of a target cell. Applicant argues that it is the numerous antibody-particle conjugates that bind to only one particular type of target cell that provide the high specificity of the claimed invention.

Applicant argues that one would not be motivated to use the method of Hajek because the methodologies are too far afield, i.e. Hajek and other are interested in detecting the majority of cells as opposed to detecting a very small number of target

cells of the same type, as Applicant does. Applicant argues that one would have to have the appropriate skills to detect a small number of cells, which required experimentation with the concentration of antibodies, the affinity of the antibodies, the amounts of particles, and conditions such as incubation time and temperature, etc.

Applicant argues that furthermore, there would be no reasonable expectation of success in modifying Hajek for example, because Hajek utilizes dead cells in their method., and that that dead cells, as are used in the method of Hajek, rupture in a suspension and could not be used in this type of method, because the antigens on the surface of the cells are destroyed, making it impossible to have optimal binding to the antibodies. Applicant argues that Applicant's method allows the cells to be collected, and used in further studies where it is necessary to have living cells.

The submission of Exhibit A is acknowledged.

Applicant's arguments in paper of 07/06/04 have been considered but are found not to be persuasive for the following reasons:

Hajek et al teach that the cells are combined with a plurality of sets of microspheres, each set having a reactant (antibody) bound specifically to a different specific molecule on at least one type of cell (claim 18). Similarly, Hajek et al teach that results are seen when a specific cell type is consistently tagged with two or more microsphere (column 9, item 8 on lines 34-39). Thus the instantly claimed notion of using different particles, with different antibodies, all directed to the same cell type is not new, and is the same as the teaching of Hajek et al.

Moreover, one would have been motivated to detect a small or normal cell range of 4-11,000 cells per microliter, because at that concentrations, the cells do not clump, as taught by Hajek et al. Further, concerning the arguments that detecting a small number of cells requires experimentation with the concentration of antibodies, the affinity of the antibodies, the amounts of particles, and conditions such as incubation time and temperature, etc, it is noted that to determine optimal conditions or concentrations of reactants is within the level of ordinary skill in the art. See In re Kronig, 190 USPQ 425.

Further, there is no indication that the cells taught by Hajek et al are ruptured and cannot be visualized with the antibodies. Hajek et al teach that the cells are stained to allow the morphology of the cells to be differentiated under a microscope in a conventional matter (column 5, lines to-62). Moreover it would have been obvious to replace the smear method taught by Hajek et al with a cell suspension that are alive, as taught by Fodstad et al, because these are conventional methods in the art to visualize cells under microscope.

B. Applicant argues that the method of Fodstad using a second set of antibodies directed to different types of cells for the same type of cells would be unusable for the instantly claimed method.

Applicant asserts that there are some apparent inconsistencies in the Exnminer's comments. On page 3, the Examiner initially indicates that Fodstad does "not preclude that the second set of antibodies could be directed to the same type of cells as the first antibody-particle complex". Then, she states "different from Applicant

interpretation... one would recognize that for increasing specificity, the second set of antibodies would be directed to a different type of cells as the first antibody-particle complexes, to distinguish different types of cells, thus increasing the specificity".

The Examiner apologizes for the inadvertent typographic error that causes the confusion.

On page 3 of previous Office action, the Examiner intended to say that "It is noted that the claims 1-4, 6-11, 13-17 are drawn to a method to detect and phenotype target cells in cell suspensions by using particles coated with "antibodies" directed against "antigenic determinants/receptors" expressed on the target cells. Thus the claims do not exclude that the second set of antibodies could be directed to different types of cells as compared to the first antibody-particle complex."

In view of such interpretation, Fodstad et al teaching would be obvious. Further, the teaching of Fodstad et al was recited to show that although Fostad et al use paramagnetic beads, the conditions taught by Fostad et al, such as duration of incubation, temperature, and the ratio of particles and tumor cells are for optimal binding between antibodies on the beads and antigens on tumor cells, and thus could be applied as well for non-paramagnetic beads, wherein the presence of iron in the paramagnetic beads would not affect the binding between antibodies on the beads and antigens on tumor cells.

C. Concerning the reference by O'briant, Applicant asserts that The Applicant's method does not attempt to compensate for anything at all, but instead detects the

expression of several antigens on single cells, but does not detect several cells due to the heterogeneity within a tumor or between tumors.

Applicant argues the Examiner notes, on page 4 of the action that Fodstad and Hajek, in combination, would have made a "person skilled in the art" "motivated to phenotype within and between tumors" is however not what Applicant is hoping to accomplish, and is not what the claims are directed to.

The arguments are not found to be persuasive. It is noted that using multiple monoclonal antibodies to compensate for heterogeneity of antigenic phenotype within tumors encompasses using multiple monoclonal antiobodies for detecting a single cell type having heterogeneity of antigenic phenotype or different phenotype of antigens on cell surface of cells within tumors, and thus encompassing the claimed method.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

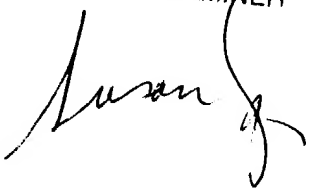
A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MINH-TAM DAVIS whose telephone number is 571-272-0830. The examiner can normally be reached on 8:30AM-5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, JEFFREY SIEW can be reached on 571-272-0787. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

SUSAN UNGAR, PH.D
PRIMARY EXAMINER



MINH TAM DAVIS

August 31, 2004